



# Reduced Risk Evaluation of Cancer

Risk Claims Evaluations Meeting July 7-10, 2003

# Lung Cancer

- The Molecular Basis of Lung Carcinogenesis  
(Fong et al. 2002, in The Molecular Basis of Human Cancer, Humana Press):
- **"It is believed that specific proto-oncogenes and tumor-suppressor genes are the target of somatic mutations in lung cancer, resulting from the genotoxic effects of tobacco smoke carcinogens."**

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# Limitations and Pitfalls

- Lung Cancer is a Focal Disease
- Target tissue specific damage
- Causation effect not clearly established with chemical carcinogenesis
- Most studies conducted in lung cancer patients

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# Imaging

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- Currently Spiral Computed topography (CT) has been used **to detect lesions** the size of  $0.3 \text{ cm}^3$

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# Circulating Tumor Markers

- Carcinoembryonic antigen (CEA)
- Squamous Cell Carcinoma Antigen (SCCA)
- Tissue polypeptide antigen
- Cytokeratin 19 and 20
- Collagen type I
- Heterogeneous nuclear ribonucleoprotein A2/B1
- Parathyroid hormone-related protein
- Neuron-specific enolase

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## **IOM Chptr 5 “Scientific Basis for PREP assessment” Table 5-4, Pg 152**

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- **Enzymatic Induction**
  - CYP1A2 enzyme induction
  - DNA repair enzymes
  - Microarray assays for mRNA expression and proteomics
- **Chromosomal Alterations**
- **Mitochondrial mutations**
- **Epigenetic cancer effects**

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# Summary of the PM Symposium on Biomarkers and Disease Models for Cancer, June 2002 at Cologne, Germany

- "Consideration should be given to the use of
  - metabonomics in both cell and whole animal studies for identification of new biomarkers of exposure, and
  - pattern recognition/bioinformatics for identification of biomarkers of effect.
- The use of oral swabs and isolation of buccal cells for biomarkers of effect (e.g., DNA adducts) should be considered, but the relevance of this surrogate tissue to the lung is unclear." Tony Tricker

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